Asian Journal of Surgery (2016) xx, 1–9

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-asianjournalsurgery.com

ORIGINAL ARTICLE

Comparison of the outcomes of hepatocellular carcinoma after hepatectomy between two regional medical centers in China and Japan

Kai Wang [a,b], Susumu Eguchi [b,*], Masaaki Hidaka [b], Tao Jin [a], Akihiko Soyama [b], Tamotsu Kuroki [b], Mingwen Huang [a], Linquan Wu [a], Shubing Zou [a], Jianghua Shao [a]

[a] *Department of Hepato-Biliary and Pancreatic Surgery, The Second Affiliated Hospital of Nanchang University, No.1 Minde Road, Nanchang 330006, PR China*
[b] *Department of Surgery, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan*

Received 18 November 2015; received in revised form 24 February 2016; accepted 1 March 2016

KEYWORDS
China;
comparison;
hepatectomy;
hepatocellular carcinoma;
Japan

Summary *Background:* Hepatocellular carcinoma (HCC) is a common malignant disease of the liver in China and Japan. The purpose of this study was to compare the outcomes of HCC patients after hepatectomy between two regional medical centers in China and Japan.
Methods: Data on HCC after hepatectomy were collected from January 2005 to December 2014 from Nagasaki University Hospital in Nagasaki, Japan and the Second Affiliated Hospital of Nanchang University in Nanchang, China. The patient and tumor characteristics, HCC etiology, and overall survival rates after hepatectomy were investigated.
Results: Two hundred patients in the Nagasaki group and 238 patients in the Nanchang group were diagnosed with HCC and underwent hepatectomy. The major underlying liver diseases were hepatitis C infection (32%, 64/200) and nonalcoholic steatohepatitis (NASH) (34.5%, 69/200) in the Nagasaki group, while in the Nanchang group, hepatitis B infection (79.4%, 189/238) was the dominant etiology. Large tumors ($>$ 5 cm), the presence of a tumor capsule and a high alpha-fetoprotein value ($\geq$ 400 U/L) were more frequently observed in the Nanchang group as compared with the Nagasaki group ($p < 0.05$). According to an outcome analysis, the Nanchang patients showed worse survival rates as compared with Nagasaki patients,

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

* Corresponding author. Department of Surgery, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan.
E-mail address: sueguchi@nagasaki-u.ac.jp (S. Eguchi).

http://dx.doi.org/10.1016/j.asjsur.2016.03.002

particularly those with American Joint Committee on Cancer stages I and III due to the aggressive character of HCC in the Nanchang group.
Conclusion: There are significant differences in the clinicopathologic features and outcomes of HCC patients from Japan and China. These differences may impact the eligibility for potentially curative therapy and the prognosis of patients with HCC.

1. Introduction

Primary liver cancer is the sixth most frequent malignancy worldwide, and it is the second leading cancer in terms of mortality, with hepatocellular carcinoma (HCC) being the most common subtype of primary liver cancer. The liver cancer incidence in Eastern Asia is the highest in the world.[1] In both China and Japan, HCC is one of the most common malignant tumors; however, in China, the predominant underlying liver disease of HCC is hepatitis B virus infection, which differs from that found in Japan. According to a nationwide survey by the Liver Cancer Study Group of Japan, although the proportion of hepatitis virus-related HCC decreased in Japan between 2005 and 2015, the HBV infection rate was 13.1%, and the HCV infection rate was 67.7%.[2] Moreover, the incidence of nonBnonC-HCC more than doubled during the same period, from 6.8% to 17.3%.[2] Different etiological assessments and treatment methods may result in different outcomes between China and Japan.

The main purpose of this study was to compare the overall survival rates of patients who underwent curative hepatectomy for HCC between China and Japan and to identify the risk factors that affect the outcome of HCC after curative hepatectomy. We used data collected from two regional medical centers: Nagasaki University Hospital, Nagasaki, Japan, and the Second Hospital affiliated of Nanchang University, Nanchang, China. Nagasaki is the capital and the largest city of Nagasaki Prefecture on the island of Kyushu in Japan. As of January 1, 2009, the estimated population was 446,007, and the total area covers 406.35 km^2. Nanchang is the capital of Jiangxi Province in southeastern China. As of 2010, ~5,042,565 individuals live in the prefecture, of which 2,357,838 live in an area comprising all five urban districts. All chief leading surgeons who made the decisions and performed surgery in both facilities had > 15 years of hepatobiliary and pancreatic surgical experience.

2. Materials and methods

2.1. Study setting and design

A retrospective review was conducted regarding the source population in the patient-information database of the Department of Surgery, Nagasaki University Hospital and the Department of Hepatobiliary and Pancreatic Surgery, Second Affiliated Hospital of Nanchang University. The charts of all patients who had a HCC diagnosis confirmed by histopathology were examined for detailed data elements that identified 200 patients (the Nagasaki group) and 238 patients (the Nanchang group) with HCC who had undergone curative hepatectomy with tumor-negative resection margins (R0 resection) as a first-line antitumor treatment between January 2005 and December 2014 in the two facilities. None of the patients had received presurgical

Table 1 Comparison of clinicopathologic characteristics.

Variable	Nagasaki group (n = 200)	Nanchang group (n = 238)	p
Gender			0.006
Male	153 (76.5)	206 (86.6)	
Female	47 (23.5)	32 (13.4)	
Age (y)			<0.001
Mean ± SD	68 ± 10.7	52 ± 12.7	
Range	31–90	17–82	
Underlying liver disease			<0.001
HBV	52 (26)	189 (79.4)	
HCV	64 (32)	0	
NASH	69 (34.5)	14 (5.9)	
Alcohol	12 (6)	1 (0.4)	
HBV-HCV	1 (0.5)	1 (0.4)	
HBV-Alcohol	1 (0.5)	33 (13.9)	
HCV-Alcohol	1 (0.5)	0	
Child-Pugh			0.809
A	188 (94)	225 (94.5)	
B	12 (6)	13 (5.5)	
C	0	0	
AFP level distribution (ng/mL)			<0.001
≤400	165 (82.5)	141 (59.2)	
>400	35 (17.5)	97 (40.8)	
Tumor size (cm)			<0.001
≤5	148 (74)	115 (48.3)	
>5	52 (26)	123 (51.7)	
Tumor numbers			0.018
≤3	197 (98.5)	224 (94.1)	
>3	3 (1.5)	14 (5.9)	
Tumor capsule			<0.001
Present	146 (73)	213 (89.5)	
Absent	54 (27)	25 (10.5)	
Vascular invasion			<0.001
Present	41 (20.5)	20 (8.4)	
Absent	159 (79.5)	218 (91.6)	

Please cite this article in press as: Wang K, et al., Comparison of the outcomes of hepatocellular carcinoma after hepatectomy between two regional medical centers in China and Japan, Asian Journal of Surgery (2016), http://dx.doi.org/10.1016/j.asjsur.2016.03.002

Table 1 (*continued*)

Variable	Nagasaki group (n = 200)	Nanchang group (n = 238)	p
Differentiation			<0.001
Well	53 (26.5)	27 (11.3)	
Moderate	119 (59.5)	162 (68.1)	
Poor	19 (9.5)	37 (15.5)	
Unknown	9 (4.5)	12 (5)	
AJCC Stage			0.010
I	132 (66)	157 (66)	
II	36 (18)	23 (9.7)	
IIIa	13 (6.5)	14 (5.9)	
IIIb	14 (7)	13 (5.5)	
IIIc	4 (2)	28 (11.8)	
IVa	1 (0.5)	3 (1.3)	
IVb	0	0	
Hepatectomy			<0.001
Anatomical	139 (69.5)	103 (43.3)	
Partial	61 (30.5)	135 (56.7)	
Mortality at 30 d	2 (1.0)	3 (1.3)	0.261

Data are presented as n (%), unless otherwise indicated.
AFP = alpha-fetoprotein; AJCC = American Joint Committee on Cancer; HBV = hepatitis B virus; HCV = hepatitis C virus; NASH = nonalcoholic steatohepatitis; SD = standard deviation.

cancer treatment or suffered from recurrence of HCC or any other known malignancy, and HCC had not metastasized to distant sites in any of the patients. The preoperative clinical and postoperative pathologic characteristics of the two groups are presented in Table 1. All patients were evaluated for HCC stage according to the 7th edition American Joint Committee on Cancer (AJCC) staging system by a retrospective analysis.[3] Ethical approval for our research protocol was obtained from the institutional review boards of both hospitals.

2.2. Criteria for hepatectomy

The patients in the Nagasaki group had been clinically evaluated and underwent curative hepatectomy according to the Nagasaki criteria described by Hidaka et al.[4] The patients in the Nanchang group had been clinically evaluated and underwent curative hepatectomy according to the guidelines of HCC diagnosis and treatment described by the Ministry of Health of the People's Republic of China.[5] All pre-, intra-, and postoperative polices followed the guidelines of the respective country as previously described.[4,5]

In this study, we attempted to compare the long-term outcomes of the patients in both institutions and identify different disease backgrounds or clinicopathologic features

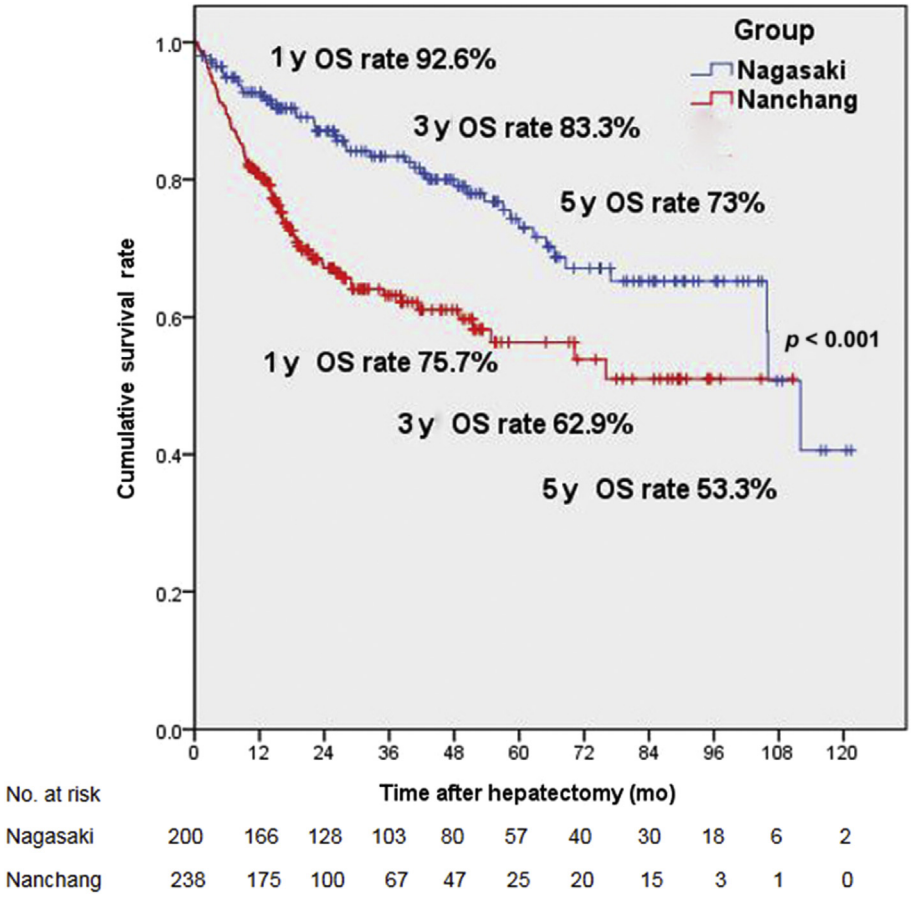

Figure 1 Overall survival after curative liver resection between the Nagasaki group and Nanchang group. OS = overall survival.

Please cite this article in press as: Wang K, et al., Comparison of the outcomes of hepatocellular carcinoma after hepatectomy between two regional medical centers in China and Japan, Asian Journal of Surgery (2016), http://dx.doi.org/10.1016/j.asjsur.2016.03.002

in the two institutions. We excluded patients who died due to the operation.

2.3. Statistical analysis

Data were analyzed using SPSS version 19 (IBM, Armonk, NY, USA). Continuous variables were expressed as medians and ranges. All results were rounded to no more than three significant figures as confirmed by our biostatistician. Categorical variables were expressed as frequencies and percentages. The Mann–Whitney *U* test was used to compare continuous variables between the two groups. The Chi-square or Fisher's exact tests was used to compare categorical variables between the two groups as appropriate. Cumulative overall survival rates were determined using the Kaplan–Meier method and compared using the Cox regression model for univariate analysis. After univariate analysis, only variables with $p < 0.1$ were included in the multivariate analysis, which used the Cox proportional hazard model to identify independent-survival predictors. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated. For all tests except the univariate analysis, a $p < 0.05$ was considered to be statistically significant.

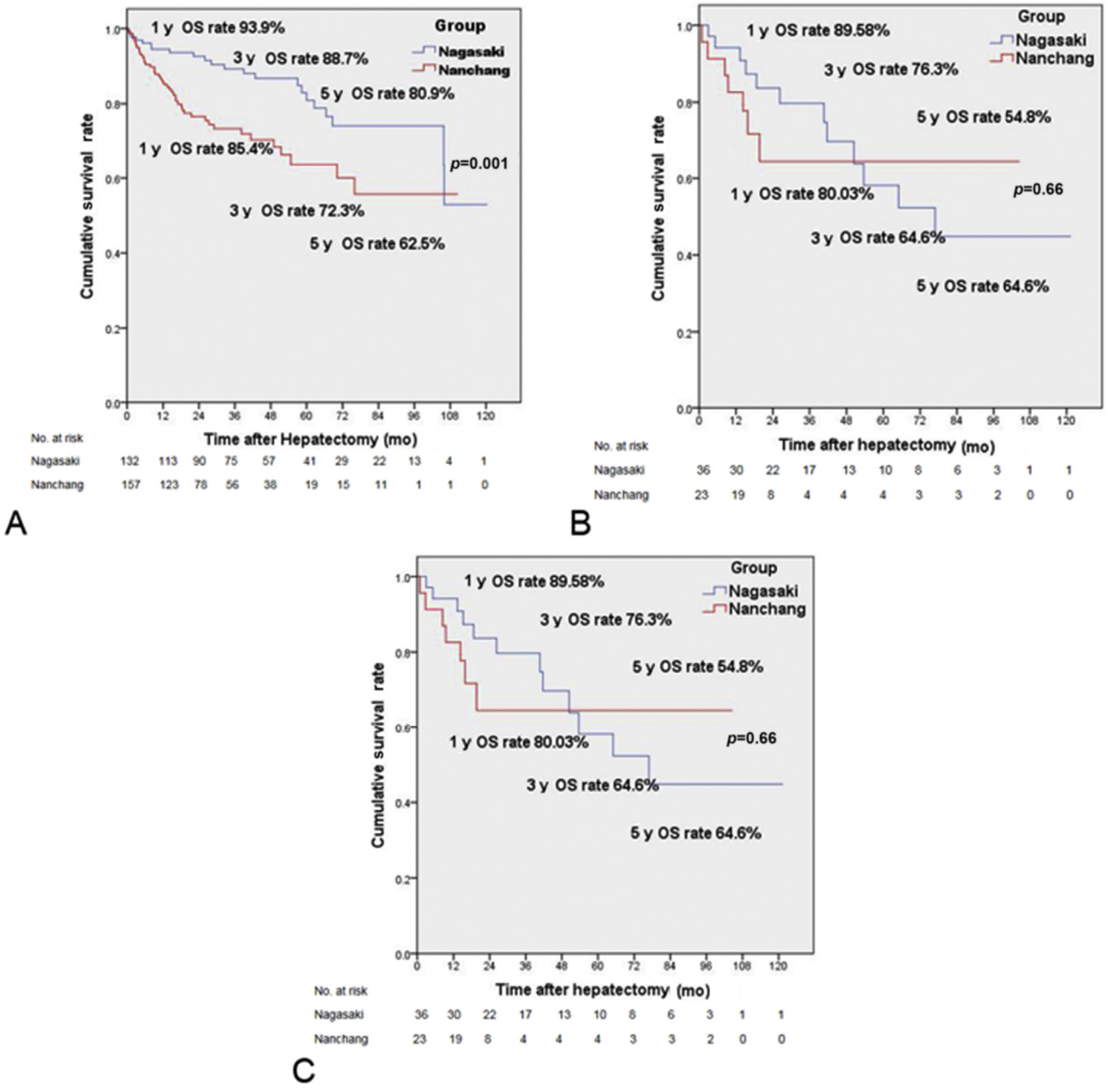

Figure 2 Overall survival after curative liver resection between the Nagasaki group and Nanchang group stratified by the AJCC stage. (A) OS of AJCC stage I comparison; (B) OS of AJCC stage II comparison; and (C) OS of beyond-AJCC stage III comparison. AJCC = American Joint Committee on Cancer; OS = overall survival.

Please cite this article in press as: Wang K, et al., Comparison of the outcomes of hepatocellular carcinoma after hepatectomy between two regional medical centers in China and Japan, Asian Journal of Surgery (2016), http://dx.doi.org/10.1016/j.asjsur.2016.03.002

3. Results

3.1. Clinicopathological characteristics of the Nagasaki group and the Nanchang group

There were significant differences in some clinicopathological variables between the two groups (Table 1). In both groups, there were more male patients than female patients; however, in the Nagasaki group, the male/female ratio was lower than that observed in the Nanchang group. There were more patients who had high levels ($>$ 400 U/L) of serum alpha-fetoprotein (AFP) in the Nanchang group as compared with the Nagasaki group. In the Nanchang group, ~51.7% of the patients had a large tumor (diameter $>$ 5 cm), whereas only 26% of the patients had a large tumor in the Nagasaki group. More patients had undergone anatomical hepatectomy in the Nagasaki group as compared with the Nanchang group, and there was no difference in the Child-Pugh score or the 30-day mortality rate between the two groups ($p = 0.261$; Table 1).

3.2. Overall survival rate analysis

The median follow-up times for the Nagasaki and Nanchang groups were 39.4 months (interquartile range, 0.6—121.4 months) and 19.6 months (interquartile range, 0.4—111 months), respectively. In the outcome analysis, the Nanchang group showed an overall worse survival rate relative to the Nagasaki group (the 1-, 3-, and 5-year overall survival rates were 75.7%, 62.9%, and 53.3% in the Nanchang group and 92.6%, 83.3%, and 73% in the Nagasaki group, respectively; $p < 0.05$; Figure 1).

3.3. Stratification and comparison of survival according to the AJCC staging system

We compared the overall survival rates of patients in the same AJCC stage between the two groups by dividing each group into three levels: AJCC stage I, AJCC stage II, and beyond-AJCC stage III. The overall survival rates of patients with AJCC stage I and those beyond-AJCC stage III in the Nagasaki group were better than those of patients in the Nanchang group (Figures 2A and 2C).

We also compared the clinicopathologic characteristics of AJCC stage I patients and those beyond-AJCC stage III between the two groups. The results showed differences between the two groups in the etiologies of patients in these two different AJCC stages (Tables 2—4). Regarding AJCC stage I, the patients tended to be older, had lower serum AFP levels, absent capsule, smaller tumor size, and better tumor differentiation in the Nagasaki group as compared with the Nanchang group. Additionally, more patients had undergone anatomical hepatectomy in the Nagasaki group as compared with the Nanchang group. Regarding the subgroup beyond-AJCC stage III, the patients tended to be older and more frequently presented with vascular invasion in the Nagasaki group as compared with the Nanchang group. For both AJCC stage I and beyond-AJCC stage III patients, more patients had undergone anatomical hepatectomy in the Nagasaki group as compared with the Nanchang group.

There was no difference in the survival rates of patients with AJCC stage II between the two groups (Figure 2B). Additionally, among AJCC stage II patients, there were significant differences in some variables between the two groups, such as age, HCC etiology, and vascular invasion (Table 3); however, there was no difference in the ratio of patients who had undergone anatomical hepatectomy between the two groups (Table 3).

3.4. Independent risks identified

In the Nagasaki group, a univariate analysis identified male gender, serum AFP level $>$ 400 U/L, absent tumor capsule, and presence of vascular invasion to be significant predictors of the survival of patients with HCC after resection (Table 5), while in the Nanchang group (Table 6), a serum AFP level $>$ 400 U/L, larger tumor size ($>$ 5 cm), vascular

Table 2 Comparison of the clinicopathological characteristics of AJCC stage I.

Variables	Nagasaki ($n = 132$)	Nanchang ($n = 157$)	p
Gender			0.077
Male	102 (77.3)	134 (85.4)	
Female	30 (22.7)	23 (14.6)	
Age (y)			<0.001
<60	24 (18.2)	108 (71.7)	
≥60	108 (81.8)	49 (31.2)	
Underlying liver disease			<0.001
HBV	29 (22)	129 (82.2)	
HCV	42 (31.8)	0	
NASH	52 (39.4)	8 (5.1)	
Alcohol	8 (6.1)	0	
HBV-HCV	0	1 (0.6)	
HBV-Alcohol	0	19 (12.1)	
HCV-Alcohol	1 (0.8)	0	
AFP (ng/mL)			<0.001
≤400	120 (90.9)	99 (63.1)	
>400	12 (9.1)	58 (36.9)	
Capsule			<0.001
Present	101 (76.5)	145 (92.4)	
Absent	31 (23.5)	12 (7.6)	
Tumor size (cm)			<0.001
≤5	110 (83.3)	84 (53.5)	
>5	22 (16.7)	73 (46.5)	
Differentiation			0.002
Well	34 (25.7)	22 (14)	
Moderate	88 (66.7)	106 (67.5)	
Poor	10 (7.6)	19 (12.1)	
Unknown	0	10 (6.4)	
Hepatectomy			0.001
Anatomical	88 (66.7)	75 (47.8)	
Partial	44 (33.3)	82 (52.2)	

Data are presented as n (%).
AFP = alpha-fetoprotein; AJCC = American Joint Committee on Cancer; HBV = hepatitis B virus; HCV = hepatitis C virus; NASH = nonalcoholic steatohepatitis.

Please cite this article in press as: Wang K, et al., Comparison of the outcomes of hepatocellular carcinoma after hepatectomy between two regional medical centers in China and Japan, Asian Journal of Surgery (2016), http://dx.doi.org/10.1016/j.asjsur.2016.03.002

invasion, and poor differentiation were significant predictors of survival. In the multivariate Cox proportional HR analysis, male gender, serum AFP > 400 U/L, and absent tumor capsule were independent-risk factors of overall survival in the Nagasaki group, whereas a larger tumor (> 5 cm), vascular invasion, and poor differentiation were independent-risk factors of overall survival in the Nanchang group.

4. Discussion

In East Asia, hepatitis virus infection is the most common cause of HCC.[6] However, there have been variations in the subtype of hepatitis infection in different countries. In China, the predominant HCC etiology is HBV related,[7] whereas in Japan, HCV infection is more common than HBV infection.[6] Furthermore, the number of nonBnonC-HCC patients has recently increased in Japan.[8] Although the epidemiologic analyses and clinical series have led to a better understanding of the behavior and natural history of HCC, these studied do not typically subanalyze the results according to the underlying liver disease; therefore, variations in the patterns of presentation, tumor biology, or treatment outcomes for HCC according to the underlying disease remain unclear.[2,6,9] According to the data presented here, we found that there were significant differences in the etiology between the population of HCC

Table 3 Comparison of the clinicopathological characteristics of AJCC stage II.

Variables	Nagasaki (n = 36)	Nanchang (n = 23)	p
Gender			0.183
Male	26 (72.2)	20 (87)	
Female	10 (27.8)	3 (13)	
Age (y)			<0.001
<60	30 (83.3)	15 (65.2)	
≥60	6 (16.7)	8 (34.8)	
Underlying liver disease			<0.001
HBV	9 (25)	18 (78.3)	
HCV	17 (47.2)	0	
NASH	5 (13.9)	3 (13)	
Alcohol	4 (11.1)	0	
HBV-HCV	1 (2.8)	0	
HBV-Alcohol	0	2 (8.7)	
HCV-Alcohol	0	0	
AFP (ng/mL)			0.647
≤400	27 (75)	16 (69.6)	
>400	9 (25)	7 (30.4)	
Capsule			0.080
Present	22 (61.1)	19 (82.6)	
Absent	14 (38.9)	4 (14.4)	
Tumor size (cm)			0.715
≤5	31 (86.1)	19 (82.6)	
>5	5 (13.9)	4 (14.4)	
Tumor numbers			0.025
≤3	34 (94.4)	17 (73.9)	
>3	2 (5.6)	6 (26.1)	
Vascular invasion			<0.001
Present	20 (44.4)	0	
Absent	16 (56.6)	23 (100)	
Differentiation			0.099
Well	11 (30.6)	2 (8.7)	
Moderate	19 (52.8)	18 (78.3)	
Poor	6 (16.7)	3 (13)	
Unknown	0	0	
Hepatectomy			0.124
Anatomical	23 (63.9)	10 (43.5)	
Partial	13 (36.1)	13 (56.5)	

Data are presented as n (%).
AFP = alpha-fetoprotein; AJCC = American Joint Committee on Cancer; HBV = hepatitis B virus; HCV = hepatitis C virus; NASH = nonalcoholic steatohepatitis.

Table 4 Comparison of the clinicopathological characteristics of beyond-AJCC stage III.

Variables	Nagasaki (n = 32)	Nanchang (n = 58)	p
Gender			0.136
Male	25 (78.1)	52 (89.7)	
Female	7 (21.9)	6 (11.3)	
Age (y)			<0.001
<60	11 (34.4)	43 (74.1)	
≥60	21 (65.6)	15 (25.9)	
Underlying liver disease			<0.001
HBV	14 (43.8)	42 (72.4)	
HCV	5 (15.6)	0	
NASH	12 (37.5)	3 (5.2)	
Alcohol	0	1 (1.7)	
HBV-HCV	0	0	
HBV-Alcohol	1 (3.1)	12 (20.7)	
HCV-Alcohol	0	0	
AFP (ng/mL)			0.299
≤400	18 (56.3)	26 (44.8)	
>400	14 (43.8)	32 (55.2)	
Capsule			0.152
Present	23 (71.9)	49 (84.5)	
Absent	9 (28.1)	9 (15.5)	
Tumor size (cm)			0.895
≤5	7 (21.9)	12 (20.7)	
>5	25 (78.1)	46 (79.3)	
Tumor numbers			0.106
≤3	31 (96.9)	50 (86.2)	
>3	1 (3.1)	8 (13.8)	
Vascular invasion			0.009
Present	19 (59.4)	20 (34.5	
Absent	13 (40.6)	38 (65.5)	
Differentiation			0.011
Well	9 (28.1)	3 (5.2)	
Moderate	19 (59.4)	38 (65.5)	
Poor	4 (12.5)	15 (25.9)	
Unknown	0	2 (3.4)	
Hepatectomy			<0.001
Anatomical	28 (87.5)	18 (31)	
Partial	4 (12.5)	40 (69)	

Data are presented as n (%).
AFP = alpha-fetoprotein; AJCC = American Joint Committee on Cancer; HBV = hepatitis B virus; HCV = hepatitis C virus; NASH = nonalcoholic steatohepatitis.

Please cite this article in press as: Wang K, et al., Comparison of the outcomes of hepatocellular carcinoma after hepatectomy between two regional medical centers in China and Japan, Asian Journal of Surgery (2016), http://dx.doi.org/10.1016/j.asjsur.2016.03.002

Table 5 Cox proportional HR analyses for overall survival in the Nagasaki group.

Variables	*n*	Univariate analysis		Multivariate analysis	
		HR (95% CI)	*p*	HR (95% CI)	*p*
Age (y)			0.417		
<60	41	1			
≥60	159	1.324 (0.672–2.610)			
Gender			0.036		0.015
Male	153	1		1	
Female	47	0.334 (0.120–0.932)		0.279 (0.099–0.780)	
Underlying liver disease			0.576		
HBV	52	1			
HCV	64	0.125 (0.016–0.997)			
NASH	69	0.121 (0.016–0.943)			
Alcohol	12	0.170 (0.022–1.300)			
HBV-HCV	1	0.156 (0.016–1.531)			
HBV-Alcohol	1	0			
HCV-Alcohol	1	0			
Child-Pugh			0.313		
A	188	1			
B	12	1.7 (0.607–4.762)			
AFP level (ng/mL)			0.005		0.001
≤400	165	1		1	
>400	35	2.615 (1.331–5.135)		2.995 (1.522–5.896)	
Tumor size (cm)			0.166		
≤5	148	1			
>5	52	1.587 (0.825–3.053)			
Tumor numbers			0.309		
≤3	197	1			
>3	3	0.355 (0.048–2.614)			
Tumor capsule			0.064		0.031
Present	146	1		1	
Absent	54	1.778 (0.968–3.268)		1.962 (1.065–3.616)	
Vascular invasion			0.014		0.155
Absent	159	1		1	
Present	41	2.201 (1.173–4.128)		1.682 (0.821–3.446)	
Differentiation			0.568		
Well					
Moderate	54	1			
Poor	126	1.474 (0.702–3.094)			
Unknown	20	1.546 (0.517–4.620)			
Hepatectomy			0.683		
Anatomical	139	1			
Partial	61	0.877 (0.466–1.649)			

AFP = alpha-fetoprotein; AJCC = American Joint Committee on Cancer; CI = confidence interval; HBV = hepatitis B virus; HCV = hepatitis C virus; HR = hazard regression; NASH = nonalcoholic steatohepatitis.

patients from Japan and China. In the Nagasaki group, > 66% of the patients had nonBnonC or HCV-related HCC. Conversely, these infections were rare in the Nanchang group. However, the etiology was not an independent-risk factor of overall survival for either group.

In this study, the overall survival rates of the Nagasaki group were better as compared with those in the Nanchang group. According to the results of univariate and multivariate analyses, the two groups exhibited different independent-risk factors for overall survival. We initially noted that there were more patients with larger tumors in the Nanchang group as compared with the Nagasaki group. We also found that anatomical hepatectomies were more frequently performed in patients with larger tumors (diameter > 5 cm) in the Nagasaki group (49/52, 94.2%) as compared with those in the Nanchang group (31/123, 25.2%), and, interestingly, the overall survival rate in the Nagasaki group was significantly better than that observed in the Nanchang group. Previous results indicated that anatomical hepatectomy conveyed a survival advantage over non-anatomical hepatectomy in HCC patients with tumors measuring < 5 cm in diameter.[10,11] We also found that in our patients with smaller tumor sizes (diameter ≤ 5 cm), the survival rates were not significantly different between the two groups, because anatomical hepatectomy was performed at a similar rate in both

Please cite this article in press as: Wang K, et al., Comparison of the outcomes of hepatocellular carcinoma after hepatectomy between two regional medical centers in China and Japan, Asian Journal of Surgery (2016), http://dx.doi.org/10.1016/j.asjsur.2016.03.002

Table 6 Cox proportional HR analyses for overall survival in the Nanchang group.

Variables	n	Univariate analysis		Multivariate analysis	
		HR (95% CI)	*p*	HR (95% CI)	*p*
Age (y)			0.829		
<60	166	1			
≥60	72	0.95 (0.594–1.518)			
Gender			0.652		
Male	206	1			
Female	32	1.164 (0.601–2.255)			
Underlying Liver disease			0.884		
HBV	189				
HCV	0				
NASH	14	1			
Alcohol	1	1.282 (0.555–2.961)			
HBV-HCV	1	0			
HBV-Alcohol	33	2.474 (0.342–17.877)			
HCV-Alcohol	0	1.114 (0.587–2.112)			
Child-Pugh			0.392		
A	225	1			
B	13	0.392 (0.096–1.596)			
AFP level (ng/mL)			0.005		0.184
≤400	141	1		1	
>400	97	1.843 (1.197–2.838)		1.359 (0.864–2.136)	
Tumor size (cm)			<0.001		0.028
≤5	115	1		1	
>5	123	2.376 (1.493–3.781)		1.721 (1.061–2.792)	
Tumor numbers			0.174		
≤3	224	1			
>3	14	1.785 (0.775–4.114)			
Tumor capsule			0.857		
Present	213	1			
Absent	25	1.066 (0.533–2.130)			
Vascular invasion			<0.001		0.003
Absent	219	1		1	
Present	19	3.817 (2.133–6.830)		2.522 (1.369–4.645)	
Differentiation			<0.001		<0.001
Well	27	1		1	
Moderate	162	3.071 (0.953–9.899)		2.840 (0.878–9.819)	
Poor	37	11.309 (3.400–37.620)		8.435 (2.498–28.480)	
Unknown	12	7.755 (2.097–28.683)		6.343 (1.698–23.697)	
Hepatectomy			0.062		0.564
Anatomical	103	1		1	
Partial	135	1.531 (0.978–2.395)		1.152 (0.712–1.863)	

AFP = alpha-fetoprotein; AJCC = American Joint Committee on Cancer; CI = confidence interval; HBV = hepatitis B virus; HCV = hepatitis C virus; HR = hazard regression; NASH = nonalcoholic steatohepatitis.

groups. Our results further suggested that anatomical hepatectomy may result in a survival benefit, even in HCC patients with larger tumors.

The AJCC staging system for HCC based on the objective situation of the patient, such as tumor size, tumor number, status of vascular invasion, local invasion, lymph nodes, and distant organ metastasis, was demonstrated to be an effective prognostic and evaluation system for the outcome of HCC patients, particularly those in the early stages.[3] However, another group suggested that the AJCC staging system, irrespective of the degree of liver damage and level of liver function, provides an inferior ability to evaluate the prognosis of HCC patients.[12–14] Therefore, conflicting results remain.[15,16] In this study, we found that patients with AJCC stage I had greater survival benefits relative to those with AJCC stage II and beyond stage III.

Comparing the overall survival rates of patients in different AJCC stages between the two groups, we found that patients in the Nagasaki groups exhibited a better survival rate, except for patients in AJCC stage II. According to the results of the clinicopathologic-characteristics comparison, we found more significantly different variables between AJCC stage I and beyond-AJCC stage III patients as compared to patients in AJCC stage II. We further

Please cite this article in press as: Wang K, et al., Comparison of the outcomes of hepatocellular carcinoma after hepatectomy between two regional medical centers in China and Japan, Asian Journal of Surgery (2016), http://dx.doi.org/10.1016/j.asjsur.2016.03.002

performed propensity score matching (data not shown) and found that the outcomes were similar when we balanced the baseline.

Unfortunately, due to complicated socioeconomic reasons, the management of recurrent HCC was heterogenized in China; therefore, a precise therapeutic procedure was lacking during the management of recurrent HCC in the Nanchang group despite the fact that treatment after recurrence affects survival.

The overall 30-day mortality of the entire cohort is shown in Table 1. Since the 30-day mortality rate did not differ between the two institutions, there should not have been a large difference in the surgical technique and strategy. Additionally, the size of the two cities indicates that both institutions were the primary tertiary referral hospital in their respective areas.

In conclusion, significant differences in the clinicopathologic features and outcomes existed among HCC patients in two different East Asian countries. These differences have an impact on the eligibility to receive potentially curative therapy and the subsequent prognosis of patients with HCC.

References

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin*. 2015; 65:87—108.
2. Utsunomiya T, Shimada M, Kudo M, et al. Nationwide study of 4741 patients with non-B non-C hepatocellular carcinoma with special reference to the therapeutic impact. *Ann Surg*. 2014; 259:336—345.
3. Chun YH, Kim SU, Park JY, et al. Prognostic value of the 7th edition of the AJCC staging system as a clinical staging system in patients with hepatocellular carcinoma. *Eur J Cancer*. 2011; 47:2568—2575.
4. Hidaka M, Takatsuki M, Soyama A, et al. Intraoperative portal venous pressure and long-term outcome after curative resection for hepatocellular carcinoma. *Br J Surg*. 2012;99: 1284—1289.
5. Ministry of Health of the People's Republic of China. Diagnosis and treatment standard of primary liver cancer (2011 edition). *Chin Clin Oncol*. 2011;16:929—946.
6. Hiotis SP, Rahbari NN, Villanueva GA, et al. Hepatitis B vs. Hepatitis C infection on viral hepatitis-associated hepatocellular carcinoma. *BMC Gastroenterol*. 2012;12:64.
7. Huang G, Lau WY, Shen F, et al. Preoperative hepatitis B virus DNA level is a risk factor for postoperative liver failure in patients who underwent partial hepatectomy for hepatitis B-related hepatocellular carcinoma. *World J Surg*. 2014;38: 2370—2376.
8. Urata Y, Yamasaki T, Saeki I, et al. Clinical characteristics and prognosis of non-B non-C hepatocellular carcinoma patients with modest alcohol consumption. *Hepatol Res*. 2016;46: 434—442.
9. Wang J, Xu LB, Liu C, Pang HW, Chen YJ, Ou QJ. Prognostic factors and outcome of 438 Chinese patients with hepatocellular carcinoma underwent partial hepatectomy in a single center. *World J Surg*. 2010;34:2434—2441.
10. Eguchi S, Kanematsu T, Arii S, et al. Comparison of the outcomes between an anatomical subsegmentectomy and a non-anatomical minor hepatectomy for single hepatocellular carcinomas based on a Japanese nationwide survey. *Surgery*. 2008;143:469—475.
11. Ishii M, Mizuguchi T, Kawamoto M, et al. Propensity score analysis demonstrated the prognostic advantage of anatomical liver resection in hepatocellular carcinoma. *World J Gastroenterol*. 2014;20:3335—3342.
12. Xu LB. Staging systems for predicting survival of patients with hepatocellular carcinoma after surgery. *World J Gastroenterol*. 2010;16:5257.
13. Ni XC, Yi Y, Fu YP, et al. Prognostic value of the Modified Glasgow Prognostic Score in patients undergoing radical surgery for hepatocellular carcinoma. *Medicine (Baltimore*. 2015; 94:e1486.
14. Nanashima A, Omagari K, Tobinaga S, et al. Comparative study of survival of patients with hepatocellular carcinoma predicted by different staging systems using multivariate analysis. *Eur J Surg Oncol*. 2005;31:882—890.
15. Yap AQ, Millan CA, Wang JH, et al. How to improve the outcome in patients with AJCC stage I hepatocellular carcinoma. *Anticancer Res*. 2014;34:3093—3103.
16. Ochiai T, Ishii H, Yamamoto Y, Marimura R, Ikoma H, Otsuji E. Significance of hepatectomy for AJCC/UICC T3 hepatocellular carcinoma. *Anticancer Res*. 2015;35:2921—2928.

Please cite this article in press as: Wang K, et al., Comparison of the outcomes of hepatocellular carcinoma after hepatectomy between two regional medical centers in China and Japan, Asian Journal of Surgery (2016), http://dx.doi.org/10.1016/j.asjsur.2016.03.002